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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/963,790	09/27/2001	Mike Farwick	32301WD230	9133

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EXAMINER	
STEADMAN, DAVID J	

ART UNIT	PAPER NUMBER
1656	

DATE MAILED: 12/11/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/963,790	FARWICK ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *03 October 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *5,9,12,34,35,37,38,40,42-44,46,48 and 51-56* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *5,9,12,34,35,37,38,40,42,46,48,53 and 54* is/are allowed.

6)☒ Claim(s) *43,51,52,55 and 56* is/are rejected.

7)☒ Claim(s) *44* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 5, 9, 12, 34-35, 37-38, 40, 42-44, 46, 48, and 51-56 are pending in the application.

[2] Applicant's amendment to the claims, filed on 3 October 2006, is acknowledged. This listing of the claims replaces all prior versions and listings of the claims in accordance with 37 CFR 1.121(c).

[3] Applicant's arguments filed on 3 October 2006 in response to the Office action mailed on 3 July 2006 have been fully considered and are deemed to be persuasive to overcome some of the rejections and/or objections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

[4] The text of those sections of Title 35 U.S. Code not included in the instant action can be found in a prior Office action.

Election/Restriction

[5] Claims 5, 9, 12, 34-35, 37-38, 40, 42, 46, 48, and 53-54 are directed to an allowable product. Pursuant to the procedures set forth in MPEP § 821.04(B), claims 55-56, directed to the process of making or using an allowable product, previously withdrawn from consideration as a result of a restriction requirement, are hereby rejoined and fully examined for patentability under 37 CFR 1.104.

Claim Objection

[6] Claim 55 is objected to as delineating step (d) twice. Appropriate correction is required.

Claim Rejections - 35 USC § 112, Second Paragraph

[7] Claim(s) 43 and 51-52 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. This rejection is necessitated by amendment.

Claim 43 (claims 51-52 dependent therefrom) is confusing in the recitation of "vector encoded by a nucleic acid molecule which consists of the nucleic acid molecule which encodes the vector." First, it is noted that the art does not recognize a vector that *encodes* a nucleic acid or a nucleic acid molecule that encodes a vector as vectors and nucleic acids are recognized in the art as encoding proteins. Second, it is unclear as to the meaning of the claim, particularly as the claim circularly defines the vector as being "encoded by a nucleic acid molecule" and the nucleic acid molecule as encoding the vector. Consequently, it is unclear as to the scope of claimed vectors. In the interest of advancing prosecution and it is suggested that applicant clarify the meaning of the claim.

Claim Rejections - 35 USC § 112, First Paragraph

[8] Claims 55-56 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to

one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection and is necessitated by amendment.

MPEP § 2163 states, "when filing an amendment an applicant should show support in the original disclosure for new or amended claims" and "[i]f the originally filed disclosure does not provide support for each claim limitation, or if an element which applicant describes as essential or critical is not claimed, a new or amended claim must be rejected under 35 U.S.C. 112, para. 1, as lacking adequate written description."

Claim 55 (claim 56 dependent therefrom) is drawn to a method for the fermentative preparation of L-amino acids comprising the steps of: a) cultivating a recombinant *Corynebacterium* or *Escherichia coli* host cell containing the recited nucleic acid of (a), (b), (c), (d), (e), and (f) of claim 55, and b) inducing expression of the nucleic acid sequence.

In the instant response at p. 7, top, applicant points to original claims 13 and 25 and the specification at pp. 17, 25, and Example 5 as supporting the claimed method. However, the examiner can find no support for the method of claims 55-56 in the specification or claims as originally filed. It is acknowledged that the specification discloses and the original claims recite a method for L-amino acid production (see, *e.g.*, specification at p. 1, paragraph 1 and original claim 13). However, the disclosed or originally claimed method requires the use of a host cell with an attenuated dead gene. The examiner can find no disclosure of a method for producing L-amino acids by "inducing expression" of a nucleic acid as recited in claims 55-56.

Applicant is invited to show support for claim 55 in the application as filed.

[9] Claims 43 and 51-52 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of he claimed invention. This is a written description rejection and is necessitated by amendment. It is noted that the instant rejection was raised in a previous Office action (see 9/12/2005 Office action) and withdrawn (see prior Office action). However, in view of the instant claim amendment, the rejection is reinstated.

Initially, it is noted that MPEP 2111.01 states that "[d]uring examination, the claims must be interpreted as broadly as their terms reasonably allow." In this case, it is unclear as to applicant's intended vector sequence or nucleic acid, which are circularly defined as noted above. As such, claim 43 has been interpreted as meaning the vector may include any additional nucleotide sequence at the 5'- and/or 3'-end(s) of the recited polynucleotide.

For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a *representative number of species* by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such

identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 states that a representative number of species means that the species which are adequately described are representative of the entire genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus. In this case, the specification discloses only a single representative species of the claimed genus of vectors, *i.e.*, a vector comprising a polynucleotide encoding SEQ ID NO:2 or the complete complement of a polynucleotide encoding SEQ ID NO:2. The specification fails to describe any additional representative species of the claimed genus of nucleic acids. While MPEP § 2163 acknowledges that in certain situations "one species adequately supports a genus", it is also acknowledges that "[f]or inventions in an unpredictable art, adequate written description of a genus which embraces widely variant species cannot be achieved by disclosing only one species within the genus". In the instant case, the recited genus of vectors encompasses species that are widely variant in both structure and function, including (but not limited to) nucleic acids encoding polypeptides that have function other than the DNA/RNA helicase activity of SEQ ID NO:2, including non-functional polypeptides. As such, the disclosure of the single representative species of vectors is insufficient to be representative of the attributes and features of all species encompassed by the claimed invention.

Given the lack of description of a representative number of vectors, the specification fails to sufficiently describe the claimed invention in such full, clear,

concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[10] Claims 43 and 51-52 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a vector comprising a polynucleotide encoding SEQ ID NO:2 or the complete complement of a polynucleotide encoding SEQ ID NO:2, does not reasonably provide enablement for all vectors as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims. This rejection is necessitated by amendment. It is noted that the instant rejection was raised in a previous Office action (see 9/12/2005 Office action) and withdrawn (see prior Office action). However, in view of the instant claim amendment, the rejection is reinstated.

It is the examiner's position that undue experimentation is required for a skilled artisan to make and/or use the entire scope of the claimed invention. Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). MPEP 2164.04 states, "[w]hile

the analysis and conclusion of a lack of enablement are based on the factors discussed in MPEP § 2164.01(a) and the evidence as a whole, it is not necessary to discuss each factor in the written enablement rejection" and that "[t]he language should focus on those factors, reasons, and evidence that lead the examiner to conclude that the specification fails to teach how to make and use the claimed invention without undue experimentation, or that the scope of any enablement provided to one skilled in the art is not commensurate with the scope of protection sought by the claims." Accordingly, the Factors most relevant to the instant rejection are addressed in detail below.

The breadth of the claims: As noted above, claim 43 (claim(s) 51-52 dependent therefrom) is interpreted as broadly encompassing a vector having any additional nucleotide sequence at the 5' and/or 3' end(s) of the recited polynucleotide. The enablement provided by the specification is not commensurate in scope with the claims with regard to broad scope of vectors as encompassed by the claims. In this case, the specification is enabling only for a vector comprising a nucleic acid encoding SEQ ID NO:2 or the complete complement of a polynucleotide encoding SEQ ID NO:2.

The state of the prior art; The level of one of ordinary skill; and The level of predictability in the art: The nucleotide sequence of an encoding nucleic acid determines the encoded protein's structural and functional properties. Predictability of which changes can be tolerated in an encoded protein's amino acid sequence and obtain the desired activity/utility requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (*i.e.*, expectedly intolerant to modification), and detailed knowledge

of the ways in which the proteins' structure relates to its function. The positions within a protein's sequence where modifications can be made with a reasonable expectation of success in obtaining a polypeptide having the desired activity/utility are limited in any protein and the result of such modifications is highly unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, *e.g.,* multiple substitutions. At the time of the invention, methods for isolating or generating variants and mutants of a given nucleic acid were known in the art. However, neither the specification nor the state of the art at the time of the invention provide the necessary guidance for altering the nucleotide sequence of SEQ ID NO:1, *i.e.,* taking as few as 30 nucleotides of SEQ ID NO:1 or the complement thereof and adding back sequence to the 5' and/or 3' ends, with an expectation of obtaining an encoded polypeptide having the desired activity/utility. At the time of the invention, there was a high level of unpredictability associated with altering a polypeptide sequence with an expectation that the polypeptide will maintain the desired activity/utility. For example, Branden et al. ("Introduction to Protein Structure", Garland Publishing Inc., New York; cited in the 9/12/2005 Office action) teach "[p]rotein engineers frequently have been surprised by the range of effects caused by single mutations that they hoped would change only one specific and simple property in enzymes" and "[t]he often surprising results of such experiments reveal how little we know about the rules of protein stability... ...they also serve to emphasize how difficult it is to design *de novo* stable proteins with specific functions" (page 247). The teachings of Branden et al. are exemplified by the reference

of Witkowski et al. (*Biochemistry* 38:11643-11650; cited in the 9/12/2005 Office action), which teaches that only a single amino acid substitution results in conversion of the parent polypeptide's activity from a beta-ketoacyl synthase to a malonyl decarboxylase (see *e.g.*, Table 1, page 11647).

The amount of direction provided by the inventor and The existence of working examples: The specification discloses only a single working example of the claimed vector, *i.e.,* a vector comprising a nucleic acid encoding SEQ ID NO:2 or the complete complement of a polynucleotide encoding SEQ ID NO:2. The specification fails to disclose any specific guidance for altering the nucleotide sequence of SEQ ID NO:1 with an expectation that the resulting variants of SEQ ID NO:1 or the complement thereof within the claimed vector will encode a polypeptide that maintains the desired activity/utility.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of isolating or generating variants of an encoding nucleic acid were known in the art at the time of the invention, it was not routine in the art to screen – by a trial and error process – for all nucleic acids having a substantial number of modifications as encompassed by the claims for those nucleic acids that encode a polypeptide having the desired activity/utility.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, and the high degree of unpredictability as evidenced by the prior art, undue experimentation would be necessary for a skilled

artisan to make and use the entire scope of the claimed invention. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 102

[11] The rejection of claim(s) 46 and 48 under 35 U.S.C. 102(b) as being anticipated by Voet et al. ("Biochemistry, 2nd Ed.," John Wiley and Sons, Inc., New York, 1995) is withdrawn in view of the amendment to the claims to limit the "complement" to being a complement over the "full-length" of the fragment of SEQ ID NO:1, wherein the fragment of SEQ ID NO:1 is defined in the claim as consisting of "at least 30 consecutive nucleotides." As such, the interpretation of claims 46 and 48 as set forth in the prior Office action as encompassing a complement of any length of the fragment no longer applies and the reference of Voet et al. fails to teach all limitations of the claims.

Interview Request

[12] Applicant's request for an interview is noted (remarks at p. 7, bottom). In the interest of customer service, the examiner will gladly accommodate an interview to discuss the outstanding issues addressed in this Office action. Applicant is invited to contact the examiner at the telephone number listed below to schedule a telephonic or personal interview at a time that is convenient for applicant.

Conclusion

[13] Status of the claims:

Claims 5, 9, 12, 34-35, 37-38, 40, 42-44, 46, 48, and 51-56 are pending.

Claims 5, 9, 12, 34-35, 37-38, 40, 42, 46, 48, and 53-54 appear to be in a condition for allowance.

Claim 44 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Claims 43, 51-52, and 55-56 are rejected.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Mon to Fri, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

David J. Steadman, Ph.D.
Primary Examiner
Art Unit 1656